

**Food and Drug Administration  
Center for Drug Evaluation and Research**

**Summary Minutes of the Dermatologic and Ophthalmic  
Drugs Advisory Committee Meeting  
July 19, 2016**

Location: FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland

Topic: The committee discussed biologics license application (BLA) 761032, brodalumab injection, a human monoclonal antibody, submitted by Valeant Pharmaceuticals Luxembourg S.a.r.l., proposed for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

These summary minutes for the July 19, 2016 meeting of the Dermatologic and Ophthalmic Drugs Advisory Committee of the Food and Drug Administration were approved on August 16, 2016.

I certify that I attended the July 19, 2016 meeting of the Dermatologic and Ophthalmic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

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/s/  
Jennifer A. Shepherd, RPh  
*Designated Federal Officer, DODAC*

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/s/  
Michael Bigby, MD  
*Chairperson, DODAC*

## Summary Minutes of the Dermatologic and Ophthalmic Drugs Advisory Committee Meeting July 19, 2016

The following is the final report of the Dermatologic and Ophthalmic Drugs Advisory Committee meeting held on July 19, 2016. A verbatim transcript will be available in approximately six weeks, sent to the Division of Dermatology and Dental Products and posted on the FDA website at:

<http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DermatologicandOphthalmicDrugsAdvisoryCommittee/ucm431514.htm>

All external requests for the meeting transcript should be submitted to the CDER Freedom of Information Office.

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The Dermatologic and Ophthalmic Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met on July 19, 2016, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Valeant Pharmaceuticals Luxembourg S.a.r.l. The meeting was called to order by Dr. Michael Bigby, MD (Chairperson). The conflict of interest statement was read into the record by Jennifer Shepherd, RPh (Designated Federal Officer). There were approximately 75 people in attendance. There was one Open Public Hearing speaker.

**Issue:** The committee discussed biologics license application (BLA) 761032, brodalumab injection, a human monoclonal antibody, submitted by Valeant Pharmaceuticals Luxembourg S.a.r.l., proposed for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

### **Attendance:**

**Dermatologic and Ophthalmic Drugs Advisory Committee Members Present (Voting):** Michael Bigby, MD (Chairperson); Ken Katz, MD, MSc, MCSE

**Dermatologic and Ophthalmic Drugs Advisory Committee Members Not Present (Voting):** Richard M. Awdeh, MD (Chairperson); Geoffrey G. Emerson, MD, PhD; Mary E. Maloney, MD; Stephen S. Feman, MD, MPH, FACS; Mildred M.G. Olivier, MD; David K. Yoo, MD

**Dermatologic and Ophthalmic Drugs Advisory Committee Member Present (Non-Voting):** Marla B. Sultan, MD, MBA (Industry Representative)

**Temporary Members (Voting):** Bonnie H. Arkus, RN (*Acting Consumer Representative*); Warren B. Bilker, PhD; Michael J. Blaha, MD, MPH; Erica Brittain, PhD; John J. DiGiovanna, MD; Lynn A. Drake, MD; Michael R. Irwin, MD; Francis E. Lotrich, MD, PhD; Stephen R. Marder, MD; Elaine H. Morrato, DrPH, MPH; Matthew V. Rudorfer, MD; Elizabeth Smith (*Patient Representative*); Ming T. Tan, PhD; Consuelo Walss-Bass, PhD; David D. Waters, MD; Julie M. Zito, PhD

**FDA Participants (Non-Voting):** Amy G. Egan, MD, MPH; Kendall A. Marcus, MD; Gary Chiang, MD, MPH; Cynthia L. LaCivita, PharmD; Simone P. Pinheiro, ScD, MSc

**Designated Federal Officer (Non-Voting):** Jennifer Shepherd, RPh

**Open Public Hearing Speaker:** Tena Brown

*The agenda proceeded as follows:*

Call to Order and Introduction of  
Committee

**Michael Bigby, MD**  
Chairperson, DODAC

Conflict of Interest Statement

**Jennifer Shepherd, RPh**  
Designated Federal Officer, DODAC

FDA Introductory Remarks

**Kendall A. Marcus, MD**  
Director  
Division of Dermatology and Dental Products (DDDP)  
Office of Drug Evaluation III (ODE III)  
Office of New Drugs (OND), CDER, FDA

**GUEST SPEAKER PRESENTATION**

**Ebrahim Haroon, MD**  
Medical Director  
Emory Behavioral Immunology Program  
Emory University, Assistant Professor  
Department of Psychiatry and Behavioral Sciences  
Emory School of Medicine

**APPLICANT PRESENTATIONS**

**Valeant Pharmaceuticals Luxembourg S.a.r.l.**

Introduction

**Tage Ramakrishna, MD**  
Chief Medical Officer  
President of Research and Development, Quality  
Valeant Pharmaceuticals

Medical Landscape

**Mark Lebwohl, MD**  
Professor and Chairman  
Kimberly and Eric J Waldman Department of Dermatology  
Icahn School of Medicine at Mount Sinai

Efficacy

**RK Pillai, PhD**  
Vice President, Head of Dermatology  
Valeant Pharmaceuticals

Safety

**Robert Israel, MD**  
Vice President, Clinical and Medical Affairs  
Valeant Pharmaceuticals

**APPLICANT PRESENTATIONS (CONT.)**

Suicidal Ideation and Behavior (SIB)	<b>Lauren B. Marangell, MD</b> Psychiatrist and President Brain Health Consultants
IL-17 Signaling and Safety	<b>James B. Trager, PhD</b> Vice President, Research Valeant Pharmaceuticals
Risk Management Overview	<b>Tage Ramakrishna, MD</b>
Benefit-Risk	<b>Kim A. Papp, MD, PhD, FRCPC</b> Founder and President Probity Medical Research
Closing	<b>Tage Ramakrishna, MD</b>
Clarifying Questions	
<b>BREAK</b>	
<b>FDA PRESENTATIONS</b>	
Clinical Pharmacology, Efficacy Overview, and Safety Assessment	<b>Gary Chiang, MD, MPH</b> Medical Officer DDDP, ODE-III, OND, CDER, FDA
Biostatistical Analysis of SIB	<b>Ling Lan, PhD</b> Biostatistics Reviewer Division of Biostatistics VII Office of Biostatistics Office of Translational Sciences, CDER, FDA
Division of Pharmacovigilance: Review of SIB	<b>Robert L. Levin, MD</b> Director Division of Pharmacovigilance I (DPV-I) Office of Pharmacovigilance and Epidemiology (OPE) Office of Surveillance and Epidemiology (OSE) CDER, FDA
Division of Epidemiology-I: Review of SIB	<b>Andrew Mosholder, MD, MPH</b> Medical Officer, Division of Epidemiology I (DEPI-I) OPE, OSE, CDER, FDA

**FDA PRESENTATIONS (CONT.)**

Division of Psychiatric Products: Review of  
SIB

**Jean Kim, MD, MA**  
Medical Officer  
Division of Psychiatry Products  
ODE-I, OND, CDER, FDA

Biostatistical Analysis of Major Adverse  
Cardiovascular Events (MACE)

**Gary Chiang , MD, MPH**

Division of Epidemiology-I: Review of  
MACE

**Andrew Mosholder, MD, MPH**

Risk Management Options for Brodalumab

**Jasminder Kumar, PharmD**  
Risk Management Analyst  
Division of Risk Management (DRISK)  
Office of Medication Error Prevention and Risk  
Management (OMEPRM)  
OSE, CDER, FDA

Clarifying Questions

**LUNCH**

Open Public Hearing

Charge to the Committee

**Kendall A. Marcus, MD**

Questions to the Committee/Committee Discussion

**BREAK**

Questions to the Committee/Committee Discussion

**ADJOURNMENT**

***Questions to the Committee:***

1. **DISCUSSION:** Discuss the safety data for brodalumab.

A. **DISCUSSION:** Do the safety data for brodalumab suggest a signal for:

- i. Suicide Ideation and Behavior (SIB)?
- ii. Major Adverse Cardiovascular Events (MACE)?

- B. **DISCUSSION:** If you believe there is a safety signal for SIB and/or MACE, comment on possible approaches to further evaluate these signals.

***Committee Discussion:** The committee did not believe that there was a safety signal for MACE. The committee acknowledged that the six completed suicides remain an unexplained issue and whether they are drug-related is subject to debate. There were varying opinions as to whether there was a safety signal for SIB; however, it was noted that clinicians and patients need to be made aware of the potential for SIB. The committee had differing opinions on requiring a registry to follow patients taking brodalumab. The committee discussed the difficulty in evaluating patients for increased suicide risk unless a clinician had expert psychiatric experience. The committee also debated as to whether or not the proposed enhanced safety communications are adequate to address the issue of six completed suicides. Please see the transcript for details of the committee discussion.*

2. **VOTE:** Is the overall benefit/risk profile of brodalumab acceptable to support approval for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.
- A. Yes, with labeling alone to manage the risks
  - B. Yes, but only if certain risk management options for SIB beyond labeling are implemented
  - C. No

Please provide a rationale for your vote. If you voted for A, please describe the labeling you would recommend to manage the risks. If you voted for B, describe the interventions or tools you believe would help mitigate the risk of SIB, in addition to labeling.

**Vote Result:** A – 4 votes            B – 14 votes            C – 0 votes

***Committee Discussion:** The majority of the panel voted that the overall benefit/risk profile of brodalumab is acceptable to support approval for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy, but only if certain risk management options for SIB beyond labeling are implemented. Of those who voted for “B”, the majority stated that they supported a registry or other post-marketing study of some type. Four committee members recommended a black box warning. Please see the transcript for details of the committee discussion.*

3. **DISCUSSION:** If you voted for approval in question #2, please comment on post-marketing studies/trials that are needed to further define the safety of brodalumab, including, but not limited to, the need for long-term studies to evaluate suicidality and cardiovascular events.

***Committee Discussion:** Several committee members stated their concerns that a mandatory registry could be a barrier to drug access for some patients, but supported a voluntary registry. One committee member expressed concern that the clinical endpoints related to SIB that the applicant has proposed to collect in the ongoing psoriasis patient registry may not be rigorous enough. Another committee member stated that patients on brodalumab may need*

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*additional clinician support, such as from a social worker or a psychologist. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 4:00 p.m.